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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,038	12/22/2000	James J. Benedict	2103.013900	4147

7590 05/13/2004

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/748,038

Applicant(s)

BENEDICT ET AL.

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 September 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 and 18 is/are allowed.
- 6) ☒ Claim(s) 1-7, 12-17 and 21-30 is/are rejected.
- 7) ☒ Claim(s) 8-10, 19 and 20 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 April 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 20010730.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

1. The Sequence Listing filed September 4, 2003 is approved.
2. The drawings filed April 9, 2001 are objected to because Figure 19B is missing. Because there was no Figure 19B in the drawings originally filed on December 22, 2000, it does not appear that this drawing can be supplied after the filing of the application without the introduction of new matter. It will be necessary to re-number Figures 19C and 19D so that they consecutively follow Figure 19A. The drawings are also objected to because SEQ ID NOS are missing from the amino acid sequences recited in Figures 15A and 15B, and because "Sialidase" is misspelled in Figures 13A and 13B. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.
3. The disclosure is objected to because of the following informalities: The status of the parent U.S. patent application at page 1, lines 3-5, should be updated. The specification at page 6, lines 6-8, refers to a Figure 19B which does not exist in this application. The figure numbers here and throughout the specification need to be re-numbered consistent with the objection to the drawings set forth in section 2 above. The paragraph at page 18, lines 1-11, should be re-written without footnotes, because patents are not printed in page format. Appropriate correction is required.
4. Claims 1-10, 12, 19, 20, 22, 29, and 30 objected to because of the following informalities: At claim 1, line 1, "so" should be changed either to "so as to" or to "to". In claims 2, 12, and 22, last line of each claim, "fibroblast" is misspelled, and the comma at the end of each line should be changed to a period. In claims 9, 19, and 29, line 7 of each claim, the semicolon after denaturant" should be deleted. Appropriate correction is required.

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5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 7, 21, 23-25, and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,211,157. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '157 patent anticipate the instant claims 1 and 21. With respect to instant claims 3-5, 7, 23-25 and 27, the '157 patent does not claim treating human tissue, does not claim administering subcutaneously, intramuscularly, or intravenously, does not claim administering discretely or continuously, and does not claim combining its mixture of proteins with a preservative or adjuvant. It would have been obvious to one of ordinary skill in the art to treat human tissue in the claimed method of the '157 patent because the claims of the '157 patent are drawn to the treatment of patients in general and because human patients are the most common type of patients in need of angiogenesis. It would have been obvious to one of ordinary skill in the art to administer the active agents in the claimed method of the '157 patent subcutaneously, intramuscularly, intravenously, discretely, or continuously, because these are known methods of administration and known dosage schedules in the pharmaceutical arts and it is routine in the pharmaceutical arts to determine all effective and

optimal methods of administration and dosage schedules. It would have been obvious to one of ordinary skill in the art to combine the active agents in the claimed method of the '157 patent with preservatives or adjuvants because these are well-known components of pharmaceutical mixtures and are routinely used for ease of storage, transportation, measurement, and administration.

6. The effective filing date of instant claims 1, 11, and 21 is deemed to be October 16, 1998, the filing date of parent application 09/173,989. Instant claims 1, 11, and 21 are deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/173,989 because the parent application '989, under the test of 35 U.S.C. 112, first paragraph discloses the claimed invention. Accordingly, Ripamonti et al (U.S. Patent Application Publication 2003/0104977) is not prior art against these claims.

The effective filing date of instant claims 2-10, 12-20, and 22-30 is deemed to be December 22, 2000, the filing date of the instant application. Instant claims 2-10, 12-20, and 22-30 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/173,989 because the parent application '989, under the test of 35 U.S.C. 112, first paragraph does not disclose a mixture of proteins which comprises at least two growth factors selected from those listed in instant claims 2, 12, and 22; does not disclose administration to a human; does not disclose subcutaneous, intramuscular, or intravenous administration; does not disclose discrete or continuous administration; does not disclose administration in combination with a preservative or an adjuvant; does not disclose a mixture of proteins which comprises those specified in instant claims 8, 18, and 28; and does not disclose obtaining the protein mixture by steps including cleaning ground bone, demineralizing cleaned ground bone, and extracting with

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protein denaturants in general. Accordingly, because U.S. Patent No. 6,211,157 has an earlier effective filing date than these claims and has a different inventive entity than these claims, U.S. Patent No. 6,211,157 is available as prior art against these claims under 35 U.S.C. 102(e). Also, Ripamonti et al (U.S. Patent Application Publication 2003/0104977) is prior art against these claims.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. v. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. *In re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976); *In re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

8. Claims 3-5, 7, 23-25, and 27 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,211,157. See the above obviousness-type double patenting rejection.

9. Claim 21 is rejected under 35 U.S.C. 102(a) and claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by the Chinese Patent 1,163,780. The Chinese Patent '780 teaches a bone growth factor extracted from natural animal bones and containing bovine BMP and bFGF, combined with a PVP carrier. The bone growth factor is administered by injection as a bone growth stimulant and for bone healing, and its mechanism of action involves stimulating capillary proliferation, i.e. angiogenesis. See, e.g., page 3, lines 1-7; page 5, lines 2-9; page 7, lines 14-16; and page 8, lines 13-17; of the attached translation. The PVP of the Chinese Patent '780 corresponds to Applicants' claimed adjuvant.

10. Claims 23-25 are rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780. Application of the Chinese Patent '780 is the same as in the above rejection of claims 21 and 27. The Chinese Patent '780 does not teach treating human tissue, does not teach administering subcutaneously, intramuscularly, or intravenously, and does not teach administering discretely or continuously. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to stimulate bone growth and bone healing in

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humans in the method of the Chinese Patent '780 because the Chinese Patent '780 is not limited to the treatment of any particular patient and because human patients are the most common type of patients in need of bone growth and bone healing. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the active agents of the Chinese Patent '780 subcutaneously, intramuscularly, intravenously, discretely, or continuously, because these are known methods of administration and known dosage schedules in the pharmaceutical arts and it is routine in the pharmaceutical arts to determine all effective and optimal methods of administration and dosage schedules.

11. Claim 26 is rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780 as applied against claims 21 and 27 above, and further in view of Hunziker (U.S. Patent No. 5,270,300). The Chinese Patent '780 does not teach combining additional growth factors such as PDGF with its active agents. Hunziker discloses combining angiogenic agents, such as PDGF- $\alpha$ , with other agents including bFGF and BMP for the treatment and repair of defects in bone. See, e.g., the abstract and claims 1-3. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to include the PDGF-  $\alpha$  of Hunziker with the active agents of the Chinese Patent '780 because the Chinese Patent '780 discloses the necessity of stimulating capillary formation, i.e. angiogenesis, for purposes of bone healing, because Hunziker's PDGF- $\alpha$  would have been expected to provide additional angiogenic activity desired by the Chinese Patent '780, and because Hunziker discloses PDGF- $\alpha$  to be useful in combination with the same types of active agents used by the Chinese Patent '780.

12. Claims 21-30 are rejected under 35 U.S.C. 102(b) as being anticipated by the Levine et al article (Annals of Plastic Surgery, Vol. 39, pages 158-168). The Levine et al article teaches

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implanting BP on a hydroxyapatite matrix into soft tissue of a rabbit. The BP is obtained from ground bovine bones by grinding, cleaning, demineralizing, extracting, ultrafiltering, anion and cation exchange chromatography, and HPLC. Upon implantation, the BP helps induce bone growth as well as the angiogenesis necessary to support bone growth. The compositions are to be used to fill in contour defects and to reconstruct osseous defects in children. See, e.g., the Abstract; page 159, column 1, last paragraph; page 159, column 2, first and second full paragraphs; and page 166, column 1, first full paragraph. With respect to instant claims 22, 26, and 28, because the BP of the Levine et al article is obtained from the same source by the same purification method and has the same angiogenic activity as the angiogenic factor recited in Applicants' claims, the two are deemed to be the same and the BP of the Levine et al article is deemed inherently to comprise the same proteins claimed by Applicants. The hydroxyapatite of the Levine et al article corresponds to Applicants' adjuvant.

13. Claims 2, 12, and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Ripamonti et al (U.S. Patent Application Publication 2003/0104977). Ripamonti et al teach inducing angiogenesis in mammals by administering a combination of a morphogenic protein and a morphogenic protein stimulator factor. Examples of situations where angiogenesis is required include wound healing, bone repair, ischemic heart disease, and ischemic peripheral vascular disease. The morphogenic protein can be BMP-3, BMP-4, BMP-5, BMP-6, and BMP-7, and the morphogenic protein stimulatory factor can be TGF- $\beta$ 1, bFGF, IGF-1, EGF, HGF, and TGF- $\alpha$ . See, e.g., the Abstract; paragraph [0003]; Examples 5 and 6; and claims 1, 6, 11, and 13-16. The above-listed morphogenic proteins and morphogenic protein stimulator factors, being identical to those specified in instant claims 2, 12, and 22, are inherently derivable from ground

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bone. This rejection assumes that Applicants' claim limitation "derived from ground bone" is a product-by-process limitation which functionally limits the types of proteins embraced by Applicants' claims, and does not constitute a positive process step which must be practiced in combination with the administering step.

14. Claims 3-7, 13-17, and 23-27 are rejected under 35 U.S.C. 103(a) as being obvious over Ripamonti et al (U.S. Patent Application Publication 2003/0104977). Application of Ripamonti et al is the same as in the above rejection of claims 2, 12, and 22. Ripamonti et al do not teach administration to a human, do not teach administering subcutaneously, intramuscularly, or intravenously, and do not teach administering discretely or continuously. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to induce angiogenesis in humans in the method of Ripamonti et al because Ripamonti et al is not limited to the treatment of any particular patient and because human patients are the most common type of patients in need of angiogenesis. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the active agents of Ripamonti et al subcutaneously, intramuscularly, intravenously, discretely, or continuously, because these are known methods of administration and known dosage schedules in the pharmaceutical arts and it is routine in the pharmaceutical arts to determine all effective and optimal methods of administration and dosage schedules.

15. Claims 11 and 18 are allowed. Claim 19 would be allowable if rewritten or amended to overcome the claim objection set forth in this Office action. Claims 8-10 and 20 would be allowable if rewritten to overcome the claim objection set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. With respect to claim

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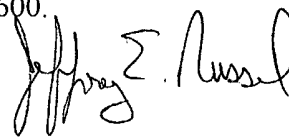
11, Ripamonti et al is not prior art, and the other prior art of record teaches angiogenesis only in the context of bone repair which does not suggest promoting vessel growth to heal a heart artery that has been partly or fully occluded. With respect to instant claims 8 and 18, Ripamonti et al do not suggest this number of and specific combination of active agents. With respect to instant claims 9, 10, 19, and 20, Ripamonti et al do not teach or suggest the purification steps required by these claims.

Marchosky (U.S. Patent No. 6,372,257) is cited as art of interest, being essentially duplicative of those references applied above which concern angiogenesis during the repair of bone.

The Ramoshebi et al article (Anatomical Record, Vol. 259, pages 97-107) is cited as art of interest, being essentially duplicative of Ripamonti et al (U.S. Patent Application Publication 2003/0104977) applied above.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (571) 272-0961. The fax number for formal communications to be entered into the record is (703) 872-9306; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel  
Primary Patent Examiner  
Art Unit 1654

JRussel  
May 7, 2004